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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/529,458 04/13/00 SHORT

J DIVER1380-1

HM12/1108

EXAMINER

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ART UNIT

PAPER NUMBER

1636

8

DATE MAILED:

11/08/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/529,458	SHORT, JAY M.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

#### **Status**

1) Responsive to communication(s) filed on \_\_\_\_\_.

2a) This action is **FINAL**.                  2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### **Disposition of Claims**

4) Claim(s) 16-47 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 16-47 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

#### **Application Papers**

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 4/13/00 is/are objected to by the Examiner.

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

#### **Priority under 35 U.S.C. § 119**

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) All b) Some \* c) None of the CERTIFIED copies of the priority documents have been:

1. received.

2. received in Application No. (Series Code / Serial Number) \_\_\_\_\_.

3. received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

#### **Attachment(s)**

15) Notice of References Cited (PTO-892)

16) Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.

18) Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.

19) Notice of Informal Patent Application (PTO-152)

20) Other: \_\_\_\_\_

### **DETAILED ACTION**

This action is in response to a request for examination of the instant application under 35 U.S.C. 371(f), having a US filing date of October 15, 1998. Claims 1-15 were cancelled in the Preliminary Amendment dated June 29, 2000. Claims 16-47, added by the same Preliminary Amendment, are pending.

#### ***Sequence Compliance***

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply fully with the requirements of 37 CFR 1.821 through 1.825 because no CRF was filed, no paper sequence was found attached to the Preliminary Amendment and no attorney statement was filed. These sequences include two primers listed on page 53. If the Sequence Listing required for the instant application is identical to that of another application, a letter may be submitted requesting transfer of the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 2422.02).

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

#### ***Drawings***

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

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3. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, in Figures 1-4, the first protein and the second protein of the first and second hybrids, the test molecule, and the detectable response, must be shown or the feature(s) canceled from the claim(s).

No new matter should be entered.

4. The drawings are objected to because in Figure 5, the word "separate" is misspelled. Correction is required.

5. In addition, Form PTO-948 summarizing the Draftsperson's review of the drawings is attached to this action.

### ***Specification***

6. The disclosure is objected to because of the following informalities: the language in the Brief Description of the Drawings does not reflect the claims language. They do not clearly refer to the first and second proteins of the first and second hybrid proteins, the test molecule or to a detectable response. On p. 11, line 18 the verb "to effect" is an apparent spelling error for the correct verb "to affect". On p. 11, lines 19-20, there is an incomplete sentence ("For instance, steroids and their receptors, or polysaccharides and their receptors.") On p. 12, lines 16-17, the phrase "potential pathways encoding bioactive molecules" is not understood; genes encode bioactive molecules. On p. 39, line 22 "Filed" should not be capitalized. On p. 53, line 12 the significance of "}{(27,}28)" is unknown. Abbreviations should be defined when first introduced in the specification,

including:  $\mu$ l, mg/ml, ng/l, Rf, kbp, mM, rRNA, U, APS, DMSO, ddH<sub>2</sub>O, EtBr, and MW.

On p.51, line 2 the word "High" in the title should be capitalized.

7. The Examples are replete with apparent errors regarding the units.

Representative examples include: p. 46, line 8 "mesh opening of 70 m"; p.46, line 9 "thickness of 70 m"; p. 47, line 16 "digest 10 l DNA....stain gel in 1 g/ml EtBr"; p. 49, line 24 "cells collected on a 0.22 m..."; p. 48, line 4 "examine 5 l of each fraction..."; p. 50, line 25 "concentration of 2.5 ng/l for ligation"; p.51, line 16 "in a 15 l ligation reaction"

8. On p. 51, lines 8-10, there is an order of magnitude error somewhere in the number of cells in 1 ml of agarose, in the number of cells in the gel slice used, or in the volume of the gel slice used, as the numbers provided are inconsistent. Specifically, if there are  $7.5 \times 10^5$  cells in a 1 ml agarose plug, and a 72  $\mu$ l slice is used, there are  $5.4 \times 10^4$  cells in that slice.

Appropriate correction is required.

9. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: "extremophiles", "thermophiles, hyperthermophiles, psychrophiles, and psychrotrophs" in claims 31 and 32 are not mentioned or described in the specification.

Appropriate correction is required.

***Claim Objections***

10. Claims 19, 20, 25 and 27 are objected to because of the following informalities:

In claim 19, "a different proteins" is improper grammar. In claim 20, "chloramphenical" is misspelled. In claim 25, "contains the first, second and third gene" is improper grammar. In claim 27, "the test molecules is derived" is improper grammar.

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 16-21 and 36-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing the method in a cell, and with gene expression of a reporter gene as the basis of the detectable signal, does not reasonably provide enablement for performing the method in a cell with a non-gene expression based detectable signal or for performing the method in vitro with either type of detectable signal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims without undue experimentation.

The disclosure does not provide teachings as to how to perform the method in vitro. How does one achieve in vitro gene expression of the two hybrid proteins, the test molecule, and of the reporter gene when that is used as the basis of the detectable

response? In addition, if the test molecule is provided in the form of a genomic expression library, how does one ascertain that only a single molecule is expressed in vitro so that the first step of "measuring the interaction ....in the presence of a *test molecule*" is achieved (emphasis added)?

The disclosure provides no detailed teachings on how to use a non-gene based detectable signal, either in a cell or in vitro. The disclosure mentions on p. 34 that mutant GFP's may provide a detectable signal not dependent on gene expression. There are no specific teachings or suggestions of what specific mutant GFP's will provide this type of function, nor the conditions in which such a signal is monitored, either in a cell or in vitro. Would any mutant green fluorescent protein suffice? Are the mutants the same or different in making the first and second hybrid proteins? Consequently, one skilled in the art would be unable to use the invention without undue experimentation.

13. Claims 45-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation. These claims present additional methods steps which have no clear connection to the method steps preceding (steps A through F) and succeeding (steps i and ii) them. Consequently, one skilled in the art would be unable to use the invention.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 16-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The first step of claim 16 cites "measuring the interaction of a first hybrid protein and a second hybrid protein" and "wherein interaction of the first protein and the second protein causes a detectable response". Is there one interaction of interest or is the second interaction, which lacks an article, a second interaction of interest? If there is only one interaction of interest, it is unclear whether it is between the first hybrid protein and second hybrid protein, or only between the first and second proteins of which the hybrids are comprised.

Claim 17 cites "the detectable response is the expression of a detectable gene". What is detected, the expression of the gene, or the gene itself? Is a "detectable gene" one for which the sequence is known so that it may be detected by, for instance, hybridization with a radioactive probe? Alternatively, is it the product of the gene or the function of that gene product that is detected? This lack of clarity renders the claim vague and indefinite.

The first step of claim 36 cites "wherein association of the first and second hybrid proteins in the absence of the test molecule results in the absence or presence of a detectable response". The second step then compares the detectable response in the presence and the absence of the test molecule. In the "absence...of a detectable response", how is the second step supposed to be achieved? If this phrase is meant to

refer to the "off" or "negative" state of a binary signal response (e.g. repression of gene expression), then claim 36 is essentially a duplicate of claim 16.

16. Claims 22-25 and 38-40 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: expression of the first, second and third recombinant genes in the host cell which is requisite for the method to succeed. If the genes encoding the two hybrid proteins are not expressed, then the two hybrid proteins will not exist therefore the method cannot be performed.

17. Claims 45-47 cite additional method steps which are not explicitly related to the method steps cited in claims on which they are dependent. Furthermore, there is the clear implication that steps G through M come after steps A through F. If steps G through M are intended to describe how to provide the test molecule of the third gene, it makes no sense that these steps would come after steps D through F.

#### ***Claim Rejections - 35 USC § 102***

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 16-26 and 36-42 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S.P. 5, 525, 490 to Erickson et al. Erickson et al discloses a method for identifying a molecule which modulates the interaction between at least a first and

second protein. See col. 3, lines 16-19. A first hybrid protein comprising a first domain and the first protein, and a second hybrid protein comprising a second domain and the second protein is taught in col. 4, lines 1-19. Measuring the interaction between the first protein and second protein in the presence and the absence of the test molecule is disclosed. See col. 7, lines 4-10. Also disclosed is method wherein the first domain is a DNA-binding moiety and the second domain is a transcriptional activator. See col. 4, lines 1-15. A detectable response based on the expression of a gene is taught in col. 3, lines 30-31 and bridge of col. 4, line 67 to col. 5, line 14. The method can be done wherein the DNA-binding moiety and the transcriptional activation moiety are derived from a single transcriptional activator (see col. 5, lines 31-34) or the two moieties are from different proteins (see col. 5, lines 34-41). Detectable genes useful for the detectable response include  $\beta$ -galactosidase, luciferase, alkaline phosphatase and genes which encode drug resistance (which covers chloramphenicol acetyl transferase). See col. 5, lines 6-15. The test molecule may be a protein or a bioactive molecule (see col. 7, lines 4-8). The method wherein the detectable gene is present in a host cell is disclosed. See col. 6, lines 27-31. The method wherein the host cell comprises a first recombinant gene encoding the first hybrid protein, a second recombinant gene encoding the second hybrid protein, or a third recombinant gene encoding the test molecule is disclosed. See col. 4, lines 15-19, and col. 15, lines 60-63. The method wherein the host cell contains both the first gene and the second gene is disclosed. See col. 4, lines 15-19. The use of a prokaryotic host is disclosed. See col. 4, lines 16-20. Thus claims 16-26 and 36-42 are anticipated by Erickson et al.

Claims 16-17, 20, 22, 23, 24, 36-39 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S.P. 5,322,801 to Kingston et al. Kingston et al discloses a method to for identifying a molecule which modulates the interaction between at least a first and second protein. See col. 3, lines 15-17. A first hybrid protein comprising a first domain and the first protein, and a second hybrid protein comprising a second domain and the second protein is taught in col. 12, lines 20-38 and col. 13, lines 8-22. Measuring the interaction between the first protein and second protein in the presence and the absence of the test molecule is disclosed. See col. 16, lines 5-47. Also disclosed is method wherein the first domain is a DNA-binding moiety and the second domain is a transcriptional repressor. See col. 12, lines 20-38. A detectable response based on the expression of a gene is taught in col. 5, lines 46-53. Detectable genes useful for the detectable response include  $\beta$ -galactosidase. See col. 5, lines 46-53. The test molecule may be a protein or a bioactive molecule (see col. 10, lines 29-34 and col. 4, lines 4-10). The method wherein the detectable gene is present in a host cell is disclosed. See col. 13, lines 8-11. The method wherein the host cell comprises a first recombinant gene encoding the first hybrid protein, a second recombinant gene encoding the second hybrid protein, or a third recombinant gene encoding the test molecule is disclosed. See col. 13, lines 8-11. The method wherein the host cell contains both the first and second recombinant genes is disclosed. See col. 13, lines 8-11. The use of a prokaryotic host is disclosed. See col. 13, lines 8-11. Thus claims 16, 17, 20, 22, 23, 24, 36-39 and 36-42 are anticipated by Kingston et al.

***Claim Rejections - 35 USC § 103***

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

22. Claims 16-26 and 36-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Erickson et al or Kingston et al in view of Mendelsohn et al (Curr. Op. in Biotech. 1994 5:482-486). Erickson et al or Kingston et al are applied as above. Neither Erickson et al nor Kingston et al explicitly discloses green fluorescent protein as the detectable gene for the detectable response as claimed in claim 17. Mendelsohn et al teaches the use of green fluorescent protein as a detectable gene in two hybrid methods used to find compounds that modulate protein interactions. See p. 485, first column. At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use green fluorescent protein as a detectable gene for a detectable response in a method for identifying a molecule which modulates the interaction between a first and second protein wherein the first protein domain is a DNA-binding moiety and the second domain is a transcriptional activator or transcriptional repressor. One of ordinary skill in the art would have been motivated to do this because Mendelsohn et al is a review article of the applications of two-hybrids systems, and the use of green fluorescent protein is suggested specifically in reference to finding compounds which modulate protein interactions by using two-hybrid systems such as

those of Erickson et al or Kingston et al. Furthermore, the use of green fluorescent protein is well known in the art for use as a reporter gene.

23. Claims 16-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Erickson et al in view Stein et al (1996 J. Bact. 178:591-599) and Horikoshi (1995 Curr. Op. in Biotech. 6:292-297). Erickson et al is applied as above. Erickson et al does not expressly disclose: the method wherein the test molecule is derived from an environmental library; the method wherein the third gene is from an environmental library; the method wherein the environmental library comprises uncultured microorganisms; the method wherein the uncultured microorganisms comprise a mixture; the method wherein the uncultured microorganisms are extremophiles; the method wherein the extremophiles are selected from the group consisting of thermophiles, hyperthermophiles, psychrophiles and psychrotrophs; the method wherein the environmental sample is enriched for prokaryotic organisms and eukaryotic organisms are selected against, isolating the nucleic acids, fractionating them and cloning them into a vector; the method wherein prior to cloning the nucleic acids are amplified. Stein et al discloses the construction of a stable environmental library from a mixture of uncultivated marine microorganisms (extremophiles) obtained as an environmental sample. Preparation of the nucleic acid involved fractionating the nucleic acids and cloning the nucleic acids into a vector. See p. 592-593. Horikoshi suggests enriching populations of extremophiles for prokaryotic organisms. See p. 294, second column wherein extremophiles are grown under hydrostatic pressures of up to 70 MPa or isolates are obtained from environments having high concentrations of organic

solvents. Enriching populations for prokaryotic organisms means one inherently reduces the population of eukaryotic organisms which thus is effectively a selection.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use the extremophile genomic library of Stein et al as the source of test molecules in the screening method of Erickson et al to identify possible modulators of protein-protein interactions. One of ordinary skill in the art would be motivated to do this because Erickson et al teaches using expression libraries, including genomic libraries (See Erickson col. 15, line 56-col. 16, line 32), to screen for modulators of protein-protein interactions. Horokoshi teaches that uncultivated microorganisms including extremophiles such as thermophiles, hyperthermophiles and psychrophiles are the source of novel biological products and their promise of possessing new genes encoding new activities. See Horikoshi, p. 292. Stein et al demonstrates that genomic libraries of extremophile microorganisms can be made.

None of the references explicitly disclose amplifying the fractionated nucleic acids prior to cloning into the vector. At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to amplify fractionated genomic nucleic acids prior to inserting them into a vector since the oligonucleotide adaptors ligated to the genomic nucleic acids to enable insertion could readily serve as primers for PCR amplification. One of ordinary skill in the art would be motivated to do this in order to increase the abundance of the genomic insert in order to increase the likelihood of efficient and comprehensive insertion.

24. Claims 16-33 and 36-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Erickson et al in view of Short et al (WO 97/04077) and Horikoshi. Erickson et al is applied as above. Erickson et al does not expressly disclose: the method wherein the test molecule is derived from an environmental library; the method wherein the third gene is from an environmental library; the method wherein the environmental library comprises uncultured microorganisms; the method wherein the uncultured microorganisms comprise a mixture; the method wherein the uncultured microorganisms are extremophiles; the method wherein the extremophiles are selected from the group consisting of thermophiles, hyperthermophiles, psychrophiles and psychrotrophs. Short et al teaches a process of screening clones having DNA from an uncultivated microorganism for a specified protein. See p. 3. Short et al additionally discloses using DNA from mixed microbial samples (p. 3), including mixed uncultured environmental samples, to form environmental DNA libraries (see p. 4). Uncultivated microorganisms include extremophiles such as thermophiles, hyperthermophiles, psychrophiles and psychrotrophs. See pp. 11. At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use the environmental library of Short et al as the source of the test molecules of Erickson et al because Erickson et al teaches the use of any expression clone libraries as the source of possible modulators of protein-protein interactions (see col. 15 line 56- col. 16, line 32). One of ordinary skill in the art would be motivated to do this because uncultivated microorganisms including extremophiles such as thermophiles, hyperthermophiles and

psychrophiles are the source of novel biological products and as such, are expected to bring many benefits to biotechnology applications. See Horikoshi, p. 292.

25. Claims 16-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Erickson et al in view Stein et al (1996 J. Bact. 178:591-599) and Horikoshi (1995 Curr. Op. in Biotech. 6:292-297), as applied to claims 16-45, and further in view of Patanjali et al (1991 Proc. Natl. Acad. Sci. 88: 1943-1947). Erickson et al, Stein et al and Horikoshi are applied as above. Erickson et al in view of Stein and Horikoshi does not explicitly teach melting the recovered fractions and allowing subsequent reannealing and amplifying any single-stranded nucleic acids present in the sample. Erickson et al teaches using cDNA expression libraries as possible sources for molecules which modulation protein-protein interactions. Patanjuli et al teaches normalizing cDNA libraries including melting nucleic acid fractions and allowing subsequent reannealing and amplifying any single-stranded nucleic acids present. See pp. 1943-1944 under Materials and Methods. At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use the normalized cDNA technique of Patanjali et al in preparing the environmental library for test molecules of Erickson et al in light of Stein et al and Horikoshi because the method of Patanjali et al is applicable to any cDNA library. One of ordinary skill in the art would be motivated to do this because the method of Patanjali et al results in normalization of a cDNA library, thus overly abundant sequences are represented in approximately the same amount as rare sequences. This is advantageous in screening for a molecule which modulates protein-protein interactions as it increases the likelihood of identifying molecules encoded by rare

sequences, and reduces the likelihood of detecting the same molecule repeatedly if it is an abundant sequence in a non-normalized cDNA library.

### ***Conclusion***

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

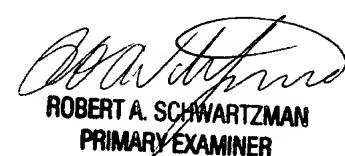
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from about 8:00 AM to about 4:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Richard Schwartz, can be reached on (703) 308-1133.

Any inquiry of a general nature or relating to the status of this application should be directed to Dianiece Jacobs, Patent Analyst whose telephone number is (703) 305-3388.

Bronwen M. Loeb  
Patent Examiner  
Art Unit 1636

November 6, 2000



ROBERT A. SCHWARTZMAN  
PRIMARY EXAMINER